method of Buckland-Wright. Radiographs were taken with an aluminium step wedge alongside in order to quantify bone density and correct for magnification of the radiograph. Joint space width (JSW), osteophyte area, subchondral sclerosis, joint angle deviation, and eminentia height were measured using the newly developed interactive Knee Images Digital Analysis (KIDA) on a standard PC.KIDA consists of several interactive steps that provide multiple measures for JSW (e.g. minimum, lateral, medial, mean), for subchondral bone density, height of the eminentia, joint angle, and osteophyte areas, all as continuous variables. The entire procedure including data storage takes less than 8 minutes per radiograph.
Two observers evaluated the radiographs on two different occasions with an interval of at least one week. The observers were blinded to the source of the radiographs and to previous measurements. Statistical analysis to compare measurements within and between observers was performed according to Bland and Altman (Lancet; 307-310, 1986). Additionally, the Kellgren & Lawrence (K&L) grade was determined and compared to individual KIDA parameters and differences in KIDA data between healthy and OA knees were evaluated.

Results: Intra- and interobserver variations for JSW, subchondral bone density, osteophytes, eminentia and joint angle were small. Observer A, e.g., found a minimum JSW of 2.8 $\pm$1.7 mm with a mean difference between two observations of -0.02 mm. Subchondral bone density was 28.6 $\pm$4.6 mm Alu Eq. with a mean difference of 0.0. Osteophyte area was 9.9 $\pm$6.8 mm^2 with a mean difference of -0.31. Several of the individual KIDA parameters correlated with the overall K&L grade (E.g. R= -0.57, 0.57, and 0.27 for minimum JSW, osteophytes, and subchondral bone density, respectively; $p<0.05$). But within one K&L grade still a large variation exists in individual KIDA parameters. Significant differences were found between healthy and OA knees (e.g. minimum JSW of 4.3 $\pm$0.6 vs. 2.2 $\pm$1.6 mm, subchondral bone density of 23.5 $\pm$5.9 vs. 32.0 $\pm$3.7 mm Alu Eq., osteophyte area of 4.1 $\pm$2.3 vs. 12.0 $\pm$6.7 mm^2 all $p<0.001$).

Conclusions: In addition to JSW measurement, objective evaluation of osteophyte formation and subchondral sclerosis (as a continuous variable) is possible on standard radiographs. The large variation in individual KIDA parameters within a single K&L grade makes KIDA evaluation more sensitive than K&L grading. On the basis of measured differences between OA and healthy individuals KIDA seems to be sensitive to detect OA changes in time, however follow-up studies to study sensitivity to change will be performed. Since the FDA demands radiographic changes to prove disease-modifying efficacy of treatment strategies, KIDA might be a worthy addition for evaluation of progression of disease in knee OA.

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THE CONTRIBUTION OF MEDIAL FEMORAL AND TIBIAL CARTILAGE THICKNESS TO MINIMUM JOINT SPACE WIDTH IN OSTEOARTHRITIC KNEES

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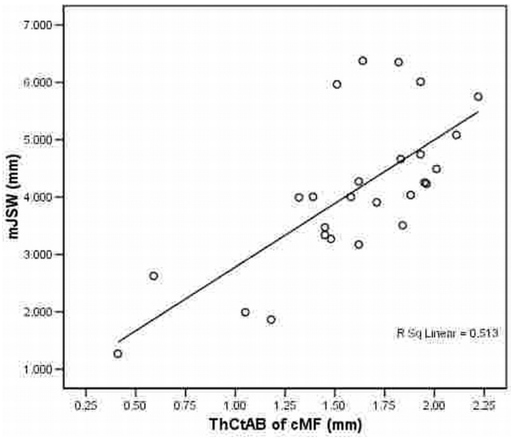
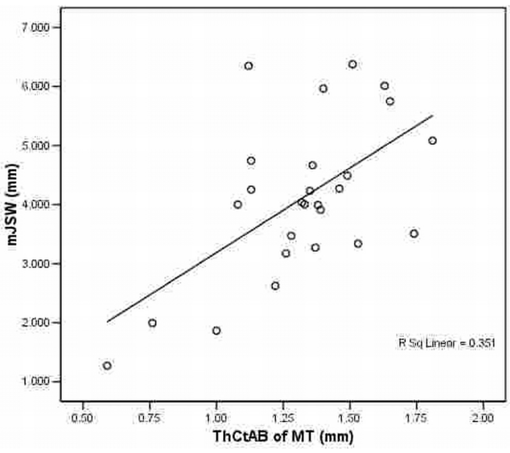
Purpose: It is understood that joint space width (JSW) measurements acquired from weight-bearing X-rays provide a surrogate measure of cartilage thickness. However, the correlation between JSW and cartilage thickness, specifically the relative contributions from the central medial femoral (cMF) and medial tibial (MT) regions, to medial mJSW in patients with knee OA has not been investigated.

Methods: We studied 26 individuals clinically diagnosed with symptomatic knee OA and a mean (SD) age of 60.1 (10.4) years and BMI of 27.6 (4.8) kg/m^2. Each volunteer underwent a fixed-flexion weight-bearing X-ray of his/her non-dominant knee. Radiographs were digitized and analyzed for medial minimum joint space width (mJSW) using an automated computer algorithm. Only those individuals with a mJSW >0 mm were included in the analyses (9 excluded). All radiographs were graded by a musculoskeletal trained radiologist using the Kellgren-Lawrence (K-L) scale. A sagittal SPGR scan (1.5 mm slice thickness) of the same knee was acquired for each participant using a 1.0 Tesla peripheral MR system (OrthOne™, ONI Inc., Wilmington, MA, USA). Articular cartilage in the cMF and MT regions was segmented by a trained technician using a validated proprietary segmentation software program (Chondrometrics GmbH, Ainring, Germany). Mean cartilage thickness (ThCtAB) was assessed in cMF and MT.

Results: K-L grading of radiographs revealed a range of OA severity; 3 grade 0, 8 grade 1, 7 grade 2, 6 grade 3 and 2 grade 4. The mean (SD) mJSW was 4.10 (1.34) mm while the mean (SD) cartilage thickness values in the cMF and MT were 1.60 (0.43) mm and 1.32 (0.28), respectively. The correlation between ThCtAB of cMF and MT was 0.66 ($p<0.01$). Regression analyses were performed to determine the amount of variation in mJSW that can be explained by the variation in ThCtAB in each of the cMF and MT. The Beta coefficient for MT was 2.87 and the R^2 was 0.351. For cMF, the Beta coefficient was 2.22 and the R^2 was 0.513. Inserted together in to the regression analysis the R^2 value was 0.539. These results suggest that roughly half (51%) of the variation in mJSW can be explained by the variation in ThCtAB in cMF and roughly one third (35%) by ThCtAB in MT (Figures 1 & 2).





Figs. 1& 2

However, since ThCtAB in the cMF and MT are correlated with one another, regression analyses performed with both MT and cMF revealed that ThCtAB variation accounts for 54% of the variation in mJSW.

Conclusions: Results from this study support the notion that joint space is indeed a surrogate measure of cartilage thickness. More importantly, however, these results provide insight into the proportion of variation in mJSW which can be accounted for by the variation in ThCtAB of the cMF and MT. While approximately half of the variation in mJSW is accounted for by variation in ThCtAB of cMF (51.3%) and approximately a third (35.0%) by MT, together ThCtAB accounts for roughly 54% of mJSW variation. Although it is not possible to discern if the remaining variation comes from other tissues or the fact that cartilage thickness values here represent mean thickness over the entire cartilage plate versus a one-dimensional measurement at one location, this is the first study to investiage the relative contributions of medial femoral and tibial cartilage thickness to mJSW in a group of individuals with knee OA.

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SUBCHONDRAL BONE MINERAL DENSITY CHANGES IN CLINICAL AND RADIOGRAPHIC OSTEOARTHRITIS OF THE KNEE: THE VIDEO STUDY

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Purpose: Changes in sub-chondral bone are common in established radiographic osteoarthritis (OA). The exact significance of these changes is uncertain and we therefore aimed to assess different regions of sub-chondral bone and their associations with both clinical and radiographic features of OA.

Methods: Subjects were patients enrolled in the VIDEO study, a 3 year randomised, double-blind, placebo controlled trial of vitamin D supplementation in symptomatic knee OA. At baseline, all subjects underwent clinical assessment using WOMAC and had knee x-rays using the MTP view. These were read using validated atlases for Kellgren-Lawrence, osteophyte and joint space narrowing scores. Subjects also had whole body, lumbar spine and total hip DXA using a Hologic Discovery instrument. In addition, participants underwent density scans of the knees in 20 degrees flexion. These were analysed using validated regions of interest to derive medial and lateral upper and lower tibial sub-chondral BMD scores.

Results: We studied 80 subjects (57% female); mean age 64.6 years, height 1.68 m and median BMI 29.0 kg/m^2. The medial sub-chondral BMD measurements were significantly higher than the lateral scores (+0.42, SD $p<0.001$) with greater upper than the lower measurements (+0.35, $p<0.001$). Females had slightly lower sub-chondral bone scores than males and, in both males and females, increasing age was associated with lower sub-chondral BMD measurements (r= -0.36, p=0.002).

There was a greater association between total hip BMD and medial compared with lateral sub-chondral measurements (R^2 = 40% and 13% respectively, p=0.036). After adjusting for age, gender and centre, increasing BMI but not height predicted medial compartment sub-chondral BMD (p=0.001). While there was little association with the pain and stiffness WOMAC sub-scales, worse functional scores did significantly ($p<0.05$) predict higher sub-chondral BMD at both the medial and lateral sites; however, this was no longer statistically significant after adjusting for total hip BMD. In this small sample, we were unable to detect differences in sub-chondral BMD by joint space narrowing or osteophyte score.

Conclusions: In this analysis of the first 80 subjects recruited to the VIDEO study, measures of sub-chondral BMD were closely correlated with hip BMD measurements and also may be associated with measures of disability.

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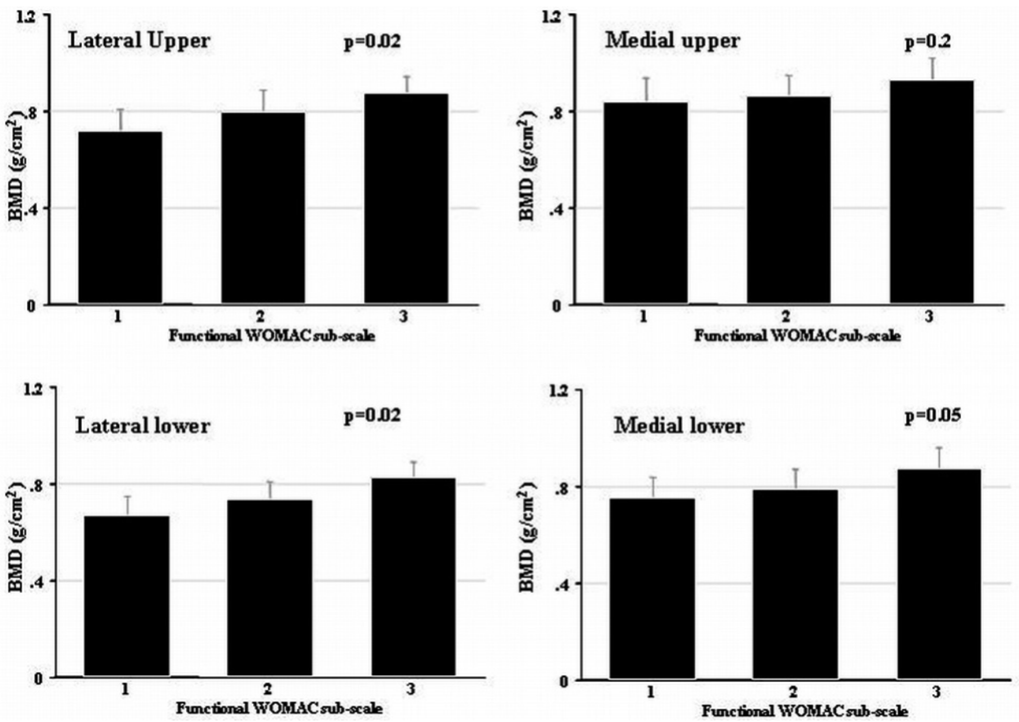

Fig. 1. Tibial regional sub-chondral BMD by increasing thirds of functional WOMAC VA sub-scale in patients with knee pain. Values are mean (95% CI).